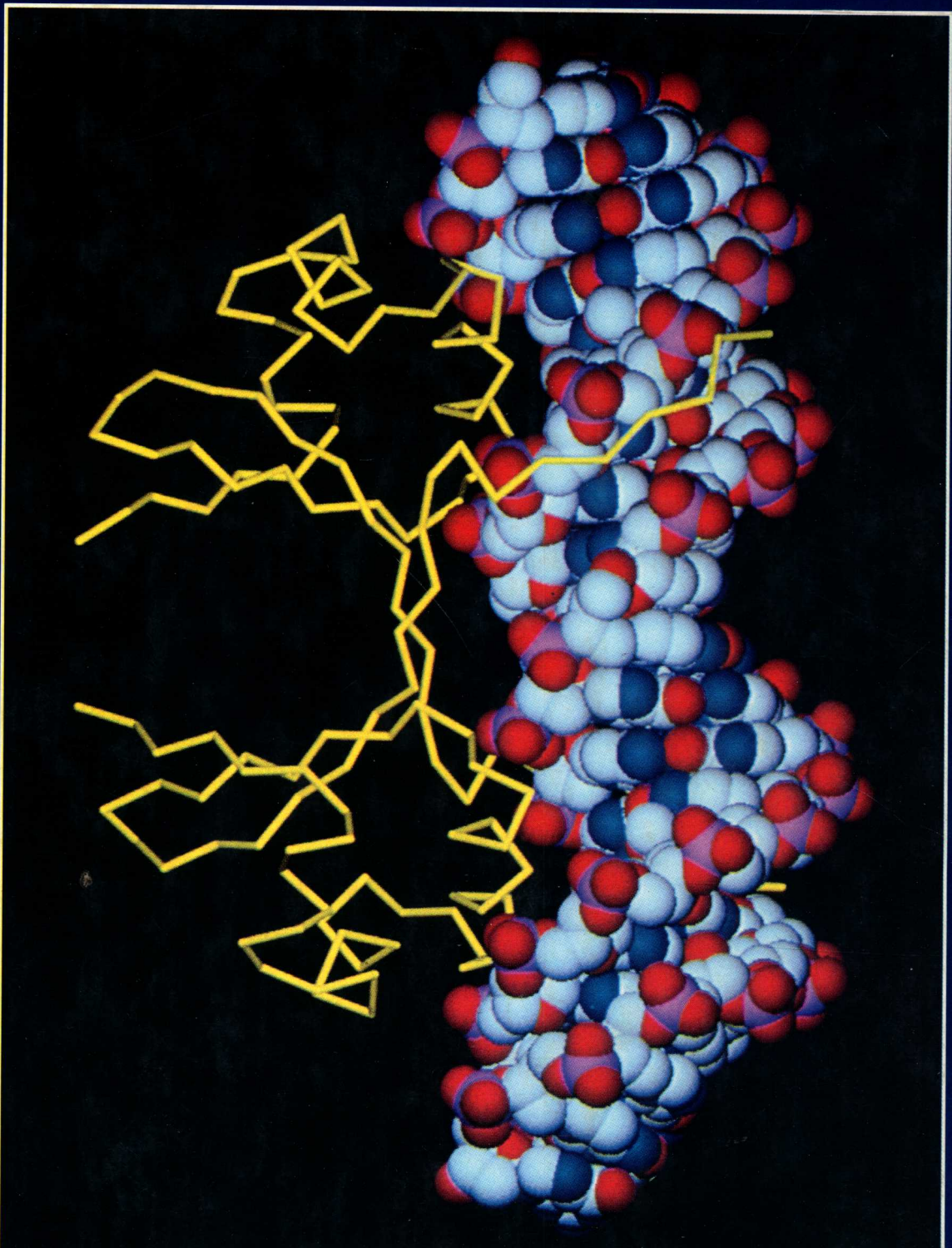


Volume II

MOLECULAR BIOLOGY OF THE GENE

WATSON ■ HOPKINS ■ ROBERTS ■ STEITZ ■ WEINER

Fourth Edition



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VOLUME II

SPECIALIZED ASPECTS

**MOLECULAR
BIOLOGY
OF THE
GENE**

FOURTH EDITION

James D. Watson

COLD SPRING HARBOR LABORATORY

Nancy H. Hopkins

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Jeffrey W. Roberts

CORNELL UNIVERSITY

Joan Argetsinger Steitz

YALE UNIVERSITY

Alan M. Weiner

YALE UNIVERSITY

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2727 Sand Hill Road
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About the Authors

James D. Watson is the Director of the Cold Spring Harbor Laboratory. He spent his undergraduate years at the University of Chicago and received his Ph.D. in 1950 from Indiana University. Between 1950 and 1953 he did postdoctoral research in Copenhagen and Cambridge, England. While at Cambridge, he began the collaboration that resulted in 1953 in the elucidation of the double-helical structure of DNA. (For this discovery, Watson, Francis Crick, and Maurice Wilkins were awarded the Nobel Prize in 1962.) Later in 1953 he went to the California Institute of Technology. He moved to Harvard in 1955, where he taught and did research on RNA synthesis and protein synthesis until 1976. While at Harvard he also wrote the first, second, and third editions of *Molecular Biology of the Gene*, which were published in 1965, 1970, and 1976, respectively. He has been at Cold Spring Harbor since 1968, where his major interest has been the induction of cancer by viruses.

Nancy H. Hopkins is a Professor of Biology at the Massachusetts Institute of Technology. She graduated from Radcliffe College in 1964 and did graduate work at Yale and Harvard, receiving her Ph.D. in Molecular Biology and Biochemistry from Harvard in 1971. After postdoctoral work at the Cold Spring Harbor Laboratory, she joined the faculty at M.I.T., where she teaches and does research on the molecular biology of retroviruses. She is the primary author of Chapters 23 through 27 in Volume II of this edition of *Molecular Biology of the Gene*.

Jeffrey W. Roberts is a Professor of Biochemistry at Cornell University. He received a B.A. in Physics and Liberal Arts from the University of Texas in 1964 and a Ph.D. in Biophysics from Harvard in 1970. He was a postdoctoral fellow at Harvard and also did research at the MRC Laboratory of Molecular Biology in Cambridge, England, before going to Cornell in 1974. His current research interests are genetic regulation in bacteria and phages, in particular the regulation of transcription and the control of DNA repair functions. He is the primary author of Chapters 11, 12, 13, 16, and 17 in Volume I of this text.

Joan Argetsinger Steitz is a Professor of Molecular Biophysics and Biochemistry at Yale University. She graduated from Antioch College in 1963 and received a Ph.D. from Harvard in 1967. She did postdoctoral work at the MRC Laboratory of Molecular Biology before joining the Yale faculty in 1970. Her research interests have always focused on the structures and functions of RNA molecules; her current research is on gene expression in mammalian cells, with an emphasis on the roles of small RNA-protein complexes. A member of the National Academy of Sciences, she is a recipient of the National Medal of Science, among other awards. She is the primary author of Chapters 14, 15, 20, and 21 in Volume I of this text.

Alan M. Weiner is a Professor of Molecular Biophysics and Biochemistry at Yale University. He graduated from Yale College in 1968 and received his Ph.D. from Harvard in 1973. After postdoctoral work at Stanford University and M.I.T., he returned to Yale as a faculty member in 1976. His current research concentrates on the structure, function, and evolution of mammalian genes for small nuclear RNA species. He is the primary author of Chapters 22 and 28 in Volume II of this text.

Preface

Today no molecular biologist knows all the important facts about the gene. This was not the case in 1965 when the first edition of *Molecular Biology of the Gene* appeared. Then there were few practicing molecular biologists and not too many facts to learn. So what we knew about DNA and RNA could easily be explained to beginning college students. That year the final codons of the genetic code were being assigned, and everyone at the forefront of research could regularly assemble in the modest lecture hall at Cold Spring Harbor. Five years later, when the second edition appeared, our numbers were rising rapidly. Yet, despite the emerging popularity of molecular biology, it was still quite uncertain if the future would be as intellectually meaningful as the years just after the discovery of the double helix. The isolation of the first repressors and the demonstration that they bind specifically to control sequences in DNA seemed to some pioneers in DNA research to mark the end of the years of germinal discovery. With no means to isolate the genes of any higher organism, much less any way to know their nucleotide sequences, any pathway to understanding how genes guide the differentiation events that give rise to multicellular organisms seemed impossibly remote.

Happily, these worries did not last long. By the time the third edition of *Molecular Biology of the Gene* was published (1976), recombinant DNA procedures had given us the power to clone genes. Moreover, there was reason to believe that highly reliable methods to rapidly sequence long stretches of DNA would soon be available. As this new era of molecular biology began, however, there initially was widely voiced concern that recombinant DNA procedures might generate dangerous and pathogenic new organisms. It was not until after much deliberation that in 1977 the cloning of the genes of higher organisms began in earnest. The third edition could barely mention the potential of recombinant DNA, and of necessity its brief discussions of how genes function in eucaryotic organisms were tentative, and sometimes quite speculative.

It is only in this fourth edition that we see the extraordinary fruits of the recombinant DNA revolution. Hardly any contemporary experiment on gene structure or function is done today without recourse to ever more powerful methods for cloning and sequencing genes. As a result, we are barraged daily by arresting new facts of such importance that we seldom can relax long enough to take comfort in the accomplishments of the immediate past. The science described in this edition is by any measure an extraordinary example of human achievement.

Because of the immense breadth of today's research on the gene, none of us can speak with real authority except in those areas where our own research efforts are concentrated. Thus it was clear from the first discussions about the fourth edition that writing it would be beyond the capability of any one scientist who also had other major responsibilities. So the task of preparing this edition has required several authors. We also realized that it would be a formidable undertaking to keep the book within a manageable length; even by adopting a larger page format, we saw no way not to exceed a thousand pages. DNA can no longer be portrayed with the grandeur it deserves in a handy volume that would be pleasant to carry across a campus. Although this edition could have been shortened by eliminating the introductory material found in the first eight chapters, we never seriously considered this alternative. To do so would remove the background material that so many readers of previous editions have found valuable, and which has let many novices in molecular biology use this book as their first real introduction to gene structure and function.

Now that we are at last finished, we find that the book is even longer than we had planned. In part this happened because we are two years behind schedule, and

150 additional pages were needed to accommodate the immediate past. We also seriously underestimated how many words and illustrations would be required to describe the extraordinary variety of gene structures and functions that underlie the complexity of eucaryotic cells. We therefore have made the decision to split the fourth edition into two volumes. In the first volume we cover the general principles that govern the structure and function of both procaryotic and eucaryotic genes. It can be used as the sole text for a one-term course in molecular biology at the undergraduate level. The second volume concentrates on those specialized aspects of the gene that underlie multicellular existence, and it concludes with a chapter on the evolution of DNA. In this edition the second volume is appreciably smaller than the first. This will not be true of subsequent editions. Now that it is at last possible to study differentiation at the DNA level, we can easily foresee the time when, in fact, more than one volume will be required for even an introductory description of how genes are organized and expressed in the specialized cells of multicellular organisms.

We hope that this new edition, like its predecessors, will be found to be a highly suitable text for teaching at the undergraduate level, and that it also will provide all molecular biologists with an easy reference to the basic facts about genes. We have shown sections of the manuscripts to a variety of colleagues who are listed as reviewers. Their comments have been taken seriously, and we hope that the final manuscript faithfully reflects their expertise. Any mistakes that remain are, of course, our responsibility. Those who have made major contributions by writing or rewriting large sections of the text are Thomas Steitz (Chapter 6), Ira Herskowitz (Chapters 18 and 19), John Coffin (Chapter 24), and Brent Cochran (Chapter 25). Their generous contributions of specialized knowledge has vastly upgraded those portions of the book. In addition, John Coffin, Scott Powers, Haruo Saito, Lisa Steiner, and Parmjit Jat helped with the references for various chapters in Volume II. The excellent index was prepared by Maija Hinkle.

Equally important have been the efforts at Cold Spring Harbor of Andrea Stephenson, whose competent secretarial assistance helped coordinate our diverse labors, and Susan Scheib, whose intelligent attention to detail kept the manuscript and the galleys moving on a forward course. We also wish to acknowledge the pleasure of working with the staff of The Benjamin/Cummings Publishing Company, including Editor-in-Chief Jim Behnke and Production Supervisors Karen Gulliver and Betsy Dileria. In particular we wish to thank Jane Gillen, who has functioned as the responsible editor during the entire writing and production of the book. An especially satisfying aspect of the process has been seeing rough drawings come alive through the efforts of the talented illustrator Georg Klatt, who has been responsible for the vast majority of the hundreds of new drawings prepared for this edition, and whose commitment and interest have greatly improved the book. And finally we gratefully acknowledge the strong support of our families throughout this endeavor, which was of course far more difficult and protracted than we ever foresaw.

James D. Watson

Nancy H. Hopkins

Jeffrey W. Roberts

Joan Argetsinger Steitz

Alan M. Weiner

Reviewers

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Manny Ares, Yale University
Spyros Artanvanis-Tsakonas, Yale University
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Bruce Stillman, Cold Spring Harbor Laboratory
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Allan Wilson, University of California-Berkeley
Barbara Wold, California Institute of Technology
Sandra Wolin, University of California-San Francisco
Keith Yamamoto, University of California-San Francisco
Jorge Yunis, University of Minnesota

Note to the Reader

The following features are intended to add to the usefulness of this book as both a text and a reference.

- **Pagination of Volumes I and II** of this text is consecutive, with the first chapter of Volume II (Chapter 22) beginning on page 745. (Cross-references refer to chapter or page numbers only.)
- **The index** at the end of this volume covers both Volumes I and II.
- **Key terms** within the text are highlighted by boldface type at the point in a chapter where the first full definition and major discussion of each term occur. Boldface type is also used in the index to identify the page where the full definition appears.
- **The concept headings**, which originated in the first edition of this text, have been retained. In addition, the longer chapters of Volume II have been subdivided into several major sections set off by briefer headings, to help organize the material for the reader. A complete list of all the headings in this volume may be found in the Detailed Contents beginning on page viii.
- **Summaries** follow the main text for each chapter.
- **Bibliographies** at the ends of the chapters provide a bridge to the scientific literature. Included are a relatively short list of recommended **General References**, which are mainly books and review articles, and a longer list of **Cited References**. The Cited References include the original papers in which important discoveries were first reported as well as a selection of more recent papers. The citations of these references within the text appear as **superscript numbers** that accompany text headings. Thus the Cited References provide a convenient way of finding more detailed information on specific topics.
- **Color plates** showing computer graphics are included in both volumes. Volume II (following p. 952) includes Immunoglobulin and Viral Hemagglutinin (Plate 7) and Capsid Structure of Icosahedral Viruses (Plate 8).

IX

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